The Declaration provided evidence that the 5'-methylene phosphonate analogs of 2'-deoxy-2'-arafluoroadenosine, and 2'-deoxy-2'-arafluorothymidine were active against Epstein Bar virus *in vitro*. The Declaration designates these compounds as **2** and **3** respectively. The Buhr et al. publication (*Collect. Czech. Chem. Commun.* 58:102-104, 1993, of record, "Buhr") provided evidence that the 5'-methylenephosphonate analog of 2'-deoxy-2'-arafluoroguanosine was active against HCMV and VZV *in vitro*. Buhr designates this compound as **9**. Applicants provided evidence of antiviral activity for the three claimed compounds and not just for one claimed compound as the Office asserted.

Turning to the claims, Applicants note that amended independent claim 51 recites (1) these three compounds, and (2) their synthetic precursors. Previously pending claims 56 and 58 recited compounds where both R^2 are hydrogen and the base B is guanine or its protected derivative N^2-isobutyrylguanine. Applicants believe that the Office should have found these two claims to be allowable. Applicants also believe that claims directed to 2'-deoxy-2'-arafluoroadenosine, and 2'-deoxy-2'-arafluorothymidine are allowable, since Applicants provided evidence in the Declaration showing their antiviral activity. Besides claiming nucleotide analogs containing protected guanine, the claims also recite the protected adenine, N^6-benzoyladenine (claims 51, 60). Claimed nucleotide analogs containing these bases are synthetic precursors for the antivirally active species as exemplified at least at specification page 10, Table 3, compound 35 and at page 13, Table 6, compound 78. Buhr also discusses using these protected bases as protected synthetic intermediates at page 103.

Applicants include with this response a Declaration by Norbert Bischofberger ("Declaration 2"), which states that it would have been readily apparent to one of ordinary skill in the art when Applicants filed the application, that species where R^2 was phenyl, alkyl (1-12C) or hydrogentriethylammonium ion, were synthetic intermediates or salts of the active compounds. The Office asserted at page 3 that Applicants provided evidence that two of the tested compounds had antiviral activity and that claimed compounds where R^2 is a group other than hydrogen might not retain antiviral activity. Compounds where R^2 is phenyl, alkyl (1-12C) or hydrogentriethylammonium ion are synthetic intermediates or salts of the active compounds. Buhr at page 103 shows the synthetic approach that Applicants used to prepare the biologically active compounds. The specification describes these

synthetic reactions for the claimed compounds, at least at Tables 3 and 6 on pages 10 and 13 and the working examples. For example, synthesis of the 2'-deoxyarafluoroguanosine diacid designated compound 80 in Table 6 (page 20) proceeds through intermediates 76, 72, 68, 61, 60, 56, 50 and 49. In intermediate 68, R^2 is phenyl and in intermediate 72 R^2 is methyl. The specification contains similar synthesis methods that use diester intermediates to make the remaining biologically active compounds that Applicants now claim. The Declaration and specification make it clear that where R^2 is phenyl or alkyl, the species are synthetic intermediates. Applicants respectfully request the Office to reconsider and withdraw the rejection.

Applicants believe the application is in condition for allowance and solicit an early Notice to that effect.

Respectfully submitted,

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